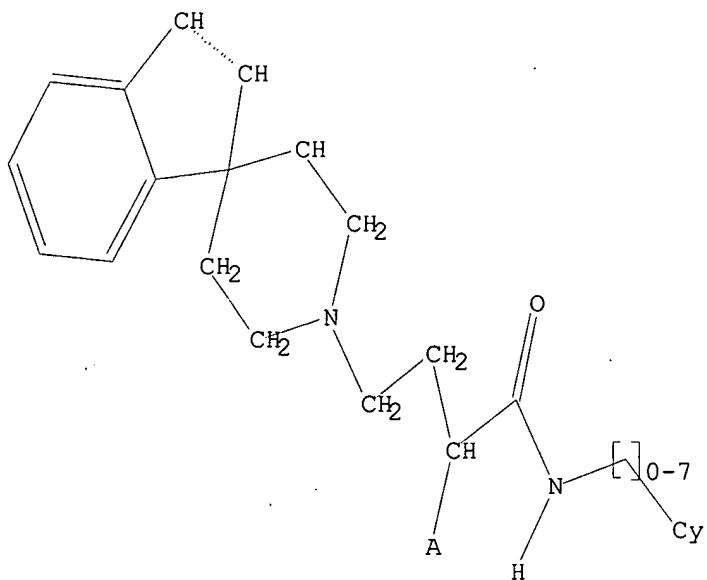


## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	290	546/17.ccls.	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/02/22 13:39
L2	1028	514/278.ccls.	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/02/22 13:39
L3	1173	l1 or l2	US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT	OR	ON	2007/02/22 13:40
L4	1154	L3	US-PGPUB; USPAT	OR	ON	2007/02/22 13:40



Structure attributes must be viewed using STN Express query preparation.

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 FULL SCREEN SEARCH COMPLETED - 479 TO ITERATE

100.0% PROCESSED 479 ITERATIONS  
 SEARCH TIME: 00.00.01

L2 21 SEA SSS FUL L1

=> fil caplus  
 COST IN U.S. DOLLARS  
 FULL ESTIMATED COST

SINCE FILE ENTRY	TOTAL SESSION
172.10	172.31

FILE 'CAPLUS' ENTERED AT 13:08:31 ON 22 FEB 2007  
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 FILE LAST UPDATED: 20 Feb 2007 (20070220/ED)

21 ANSWERS

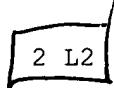
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02/22/2007

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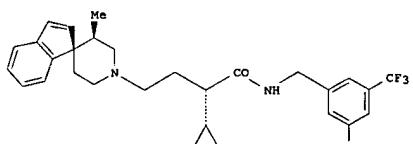
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L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN  
 ACESSION NUMBER: 2006-830241 CAPLUS  
 DOCUMENT NUMBER: 145-327676

TITLE: 4-Amino-2-alkyl-butyramides as small molecule CCR2 antagonists with favorable pharmacokinetic properties  
 AUTHOR(S): Butora, Gabor; Morriello, Gregori J.; Kothandaraman, Shankaran; Guiadeen, Deodialasingh; Pasternak, Alexander; Parsons, William H.; MacCoss, Malcolm; Viciario, Pasquale P.; Cascieri, Margaret A.; Long, Lihua  
 CORPORATE SOURCE: Merck Research Laboratories, Rahway, NJ, 07065, USA  
 SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(18), 4715-4722  
 PUBLISHER: Elsevier B.V.  
 DOCUMENT TYPE: CODEN: BMCLB; ISSN: 0960-894X  
 LANGUAGE: English  
 GI



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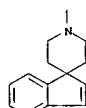
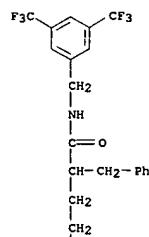
AB A systematic examination of the central aromatic portion of the lead (*2S*)-*N*-(3,5-bis(trifluoromethyl)benzyl)-2-(4-fluorophenyl)-4-(1*H*-spiro[indene-1,4'-piperidin]-1'-yl)butanamide (9) led to the discovery of a novel class of CCR2 receptor antagonists, which carry small alicyclic groups such as cyclopropyl, cyclobutyl, or cyclopropylmethyl attached at

C2 of the carbon backbone. The most potent compound discovered, namely (*2S*)-*N*-(3,5-bis(trifluoromethyl)benzyl)-2-cyclopropyl-4-[(1*R*,3*R*)-3-methyl-1*H*-spiro[indene-1,4'-piperidin]-1'-yl]butanamide (1), showed very high binding affinity (*IC50* = 4 nM, human monocyte) and excellent selectivity toward other related chemokine receptors. The excellent pharmacokinetic profile of this new lead compound allows for extensive in vivo evaluation.

IT 691874-50-7P 691874-50-9P 691874-61-0P  
 691874-66-5P 691875-74-8P 691875-75-9P  
 909717-55-1P 909717-56-2P 909717-57-3P  
 909717-58-4P 909717-61-9P 909717-62-0P  
 909717-63-1P 909717-64-2P 909717-65-3P

L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)  
 909717-66-4P 909717-67-5P 909717-73-3P  
 RL: PA (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (amino alkyl butyramides as CCR2 antagonists with favorable pharmacokinetic properties)  
 RN 691874-50-7 CAPLUS  
 CN Spiro[1*H*-indene-1,4'-piperidine]-1'-butanamide, *N*-[(3,5-bis(trifluoromethyl)phenyl)methyl]-*α*-(phenylmethyl)- (9CI) (CA INDEX NAME)

PAGE 1-A

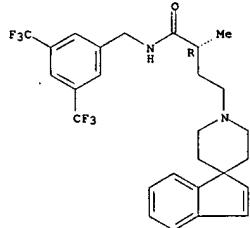


PAGE 2-A

RN 691874-60-9 CAPLUS  
 CN Spiro[1*H*-indene-1,4'-piperidine]-1'-butanamide, *N*-[(3,5-

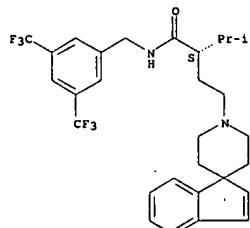
L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)  
 bis(trifluoromethyl)phenyl)methyl]-*α*-methyl-, (*αR*)- (CA INDEX NAME)

Absolute stereochemistry.



RN 691874-61-0 CAPLUS  
 CN Spiro[1*H*-indene-1,4'-piperidine]-1'-butanamide, *N*-[(3,5-bis(trifluoromethyl)phenyl)methyl]-*α*-(1-methylethyl)-, (*αS*)- (9CI) (CA INDEX NAME)

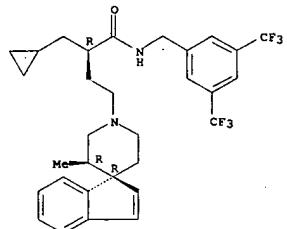
Absolute stereochemistry.



RN 691874-66-5 CAPLUS  
 CN Spiro[1*H*-indene-1,4'-piperidine]-1'-butanamide, *N*-[(3,5-bis(trifluoromethyl)phenyl)methyl]-*α*-(cyclopropylmethyl)-3'-methyl-, (*αR*,*1R*,*3R*)- (9CI) (CA INDEX NAME)

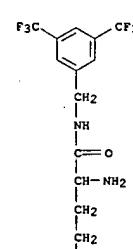
Absolute stereochemistry.

L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 691875-74-8 CAPLUS  
 CN Spiro[1*H*-indene-1,4'-piperidine]-1'-butanamide, *α*-amino-*N*-[(3,5-bis(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)

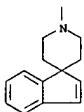
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L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

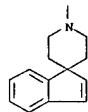
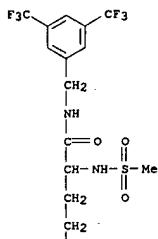
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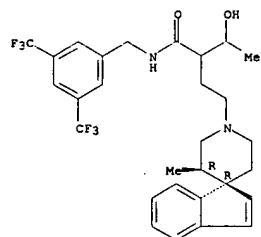
RN 691875-75-9 CAPLUS  
 CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[(3,5-bis(trifluoromethyl)phenyl)methyl]- $\alpha$ -(methylsulfonyl)amino- (9CI) (CA INDEX NAME)

PAGE 1-A



RN 909717-55-1 CAPLUS  
 CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[(3,5-bis(trifluoromethyl)phenyl)methyl]- $\alpha$ -(1-hydroxyethyl)-3'-methyl-, (1R,3'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

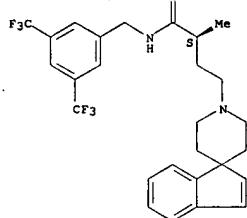


RN 909717-56-2 CAPLUS  
 CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[(3,5-bis(trifluoromethyl)phenyl)methyl]- $\alpha$ -methyl-, (aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

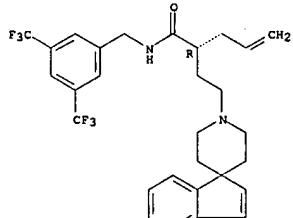
L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

(Continued)



RN 909717-57-3 CAPLUS  
 CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[(3,5-bis(trifluoromethyl)phenyl)methyl]- $\alpha$ -2-propenyl-, (aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

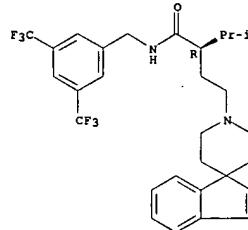


RN 909717-58-4 CAPLUS  
 CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[(3,5-bis(trifluoromethyl)phenyl)methyl]- $\alpha$ -(1-methylethyl)-, (aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

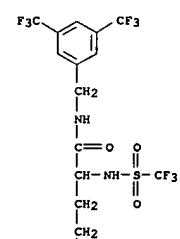
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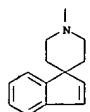
RN 909717-61-9 CAPLUS  
 CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[(3,5-bis(trifluoromethyl)phenyl)methyl]- $\alpha$ -[(trifluoromethyl)sulfonyl]amino- (9CI) (CA INDEX NAME)

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L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

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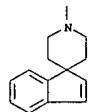


RN 909717-62-0 CAPLUS  
 CN Carbamic acid, [1-([(3,5-bis(trifluoromethyl)phenyl)methyl]amino]carbonyl)-3-spiro[1H-indene-1,4'-piperidin]-1'-ylpropyl)-, methyl ester (9CI)  
 (CA INDEX NAME)

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L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

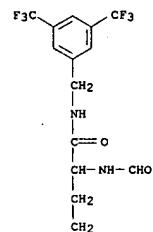
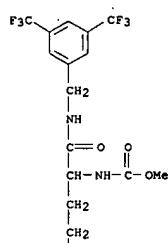
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RN 909717-63-1 CAPLUS  
 CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[(3,5-bis(trifluoromethyl)phenyl)methyl]- $\alpha$ -(formylamino)- (9CI) (CA INDEX NAME)

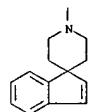
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PAGE 1-A

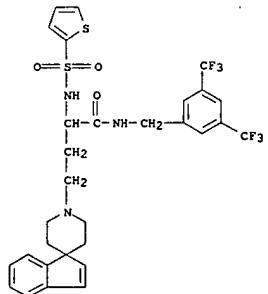


L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

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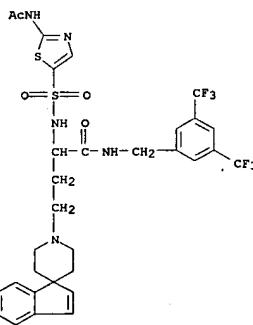
RN 909717-64-2 CAPLUS  
 CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[(3,5-bis(trifluoromethyl)phenyl)methyl]- $\alpha$ -((2-thienylsulfonyl)amino)- (9CI) (CA INDEX NAME)



RN 909717-65-3 CAPLUS  
 CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide,  $\alpha$ -[(2-(acetylamino)-5-thiazolyl)sulfonyl]amino]-N-[(3,5-bis(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)

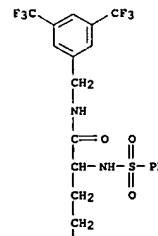
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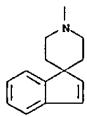
L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 909717-66-4 CAPLUS  
 CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[(3,5-bis(trifluoromethyl)phenyl)methyl]- $\alpha$ -((phenylsulfonyl)amino)- (9CI) (CA INDEX NAME)

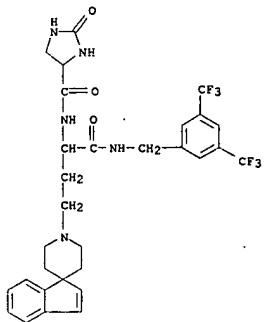
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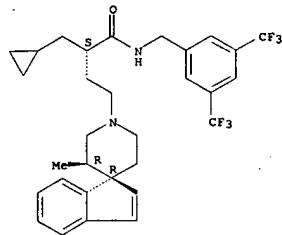
PAGE 2-A

RN 909717-67-5 CAPLUS  
 CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[(3,5-bis(trifluoromethyl)phenyl)methyl]- $\alpha$ -(1-(2-oxo-4-imidazolidinyl)carbonyl)amino]- (9CI) (CA INDEX NAME)



RN 909717-73-3 CAPLUS  
 CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[(3,5-bis(trifluoromethyl)phenyl)methyl]- $\alpha$ -(cyclopropylmethyl)-3'-methyl-, (aS,1R,3'R)- (9CI) (CA INDEX NAME)

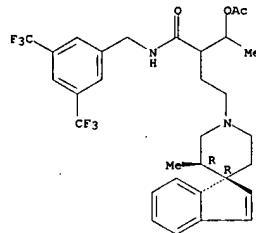
Absolute stereochemistry.



IT 909717-54-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (amino alkyl) butyramides as CCR2 antagonists with favorable pharmacokinetic properties

RN 909717-54-0 CAPLUS  
 CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide,  $\alpha$ -(1-(acetoxy)ethyl)-N-[(3,5-bis(trifluoromethyl)phenyl)methyl]-3'-methyl-, (1R,3'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

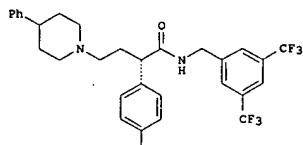
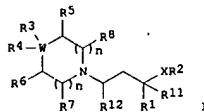
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RW: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TZ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2503720	A1	20040521	CA 2003-2503720	20031024
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EP 1558250	A1	20050803	EP 2003-75103	20031024
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, FR, BG, CY, ES, RU, SK				
JP 2006511500	T	20060406	JP 2004-550131	20031024
US 2005261325	A1	20051124	US 2005-528329	20050318
PRIORITY APPLN. INFO.:			US 2002-422268P	P 20021030
			WO 2003-US34009	W 20031024

OTHER SOURCE(S): MARPAT 140:423589  
 GI

Instant App

L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

(Continued)



II

AB Title compds. [I: W = C, N, O; X = NR10, O, CH2O, CONR10, CO2, etc.; R10 = H, (substituted) alkyl, Ph, PhCH2, alkyl, cycloalkyl; R1 = H, (substituted) alkyl-Y-Ph, alkyl-Y-heterocyclyl, etc.; Y = bond, O, S, SO, SO2, NH10; R2 = (substituted) alkylphenyl, alkylheterocyclyl; R3 = H, (substituted) alkylphenyl, alkylheterocyclyl, CF3, cycloalkyl, etc.; R4 = H, OH, alkyl, alkoxy, amino, etc.; R9R4 = atoms to form (substituted) indene, benzofuran, isobenzofuran, benzothiophuran, isobenzofuran rings; R5-R8 = H, OH, alkyl, alkoxy, O, halo, CF3, CO2R5, etc.; R9 = H, (substituted) alkyl, cycloalkyl, Ph, PhCH2; R3R5, R4R6, R5R6, R7R8 = atoms to form (substituted) rings; R11 = H, halo, alkyl, OH, alkoxy, NR9R10, etc.; R12 = H, alkyl, CO2R9; n = 0-3], were prepared. Thus, title compound (II) was prepared by reaction of 4-phenylpiperidine with the corresponding aldehyde in the presence of Na(OAc)3BH. I bound to CCR-2 receptor with IC50 5.1  $\mu$ M.

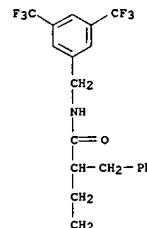
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

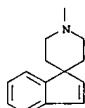
(Preparation of piperidinylbutyramides and related compds. as modulators of CCR-2 chemokine receptor activity)

RN 691874-50-7 CAPLUS  
CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[(3,5-bis(trifluoromethyl)phenyl)methyl]- $\alpha$ -(phenylmethyl)- (9CI) (CA INDEX NAME)

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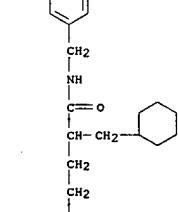
PAGE 2-A



RN 691874-52-9 CAPLUS  
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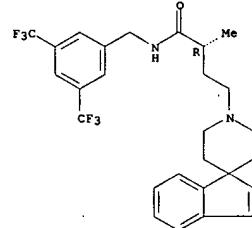
L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

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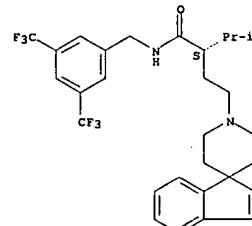
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L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 691874-61-0 CAPLUS  
CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[(3,5-bis(trifluoromethyl)phenyl)methyl]- $\alpha$ -(1-methylethyl)-, (as)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 691874-60-9 CAPLUS  
CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[(3,5-bis(trifluoromethyl)phenyl)methyl]- $\alpha$ -methyl-, (aR)- (9CI) (CA INDEX NAME)

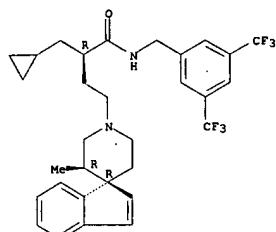
Absolute stereochemistry.

RN 691874-66-5 CAPLUS  
CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[(3,5-bis(trifluoromethyl)phenyl)methyl]- $\alpha$ -(cyclopropylmethyl)-3'-methyl-, (aR,IR,3'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

(Continued)



RN 691875-72-6 CAPLUS

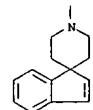
CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[(3,5-bis(trifluoromethyl)phenyl)methyl]- $\alpha$ -methoxy- (9CI) (CA INDEX NAME)

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L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

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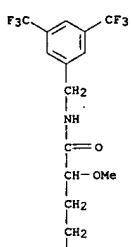
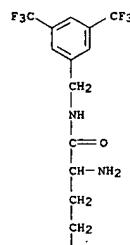
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RN 691875-74-8 CAPLUS

CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide,  $\alpha$ -amino-N-[(3,5-bis(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)

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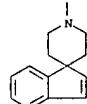
L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

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L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

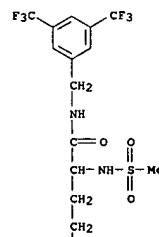
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



RN 691875-75-9 CAPLUS

CN Spiro[1H-indene-1,4'-piperidine]-1'-butanamide, N-[(3,5-bis(trifluoromethyl)phenyl)methyl]- $\alpha$ -[(methylsulfonyl)amino]- (9CI) (CA INDEX NAME)

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